5th World Congress on

BREAST CANCER

June 15-17, 2017 London, UK

Scientific Tracks & Abstracts

Day 1

Breast Cancer 2017

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Breast Cancer Therapy, Prevention and Management | Breast Cancer- Present Perspective | Breast Cancer Nursing

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Steven M Hill
Tulane University School of Medicine, USA

Session Co-chair
Manjeet Rao
University of Texas Health Science Center, USA

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Manjeet Rao, University of Texas Health Science Center, USA

Title: **The effect of Internet-based breast cancer patient's pathway on breast cancer patients' empowering process**

Anne Ryhanen, The University of Turku, Finland

Title: **Relationships among body mass index, systemic immune-inflammation index and luminal subtype in the resistance to endocrine therapy of breast cancer**

Qingxia Li, Hebei General Hospital, China

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FOXK2 aberration in breast cancers

Amy Hong Zhang
University of Texas, USA

The chromosome 17 is a frequent site of cancer-associated genetic anomalies and is strongly associated with poor prognosis. Previous studies of breast cancer have revealed the amplification of several genomic regions on 17q. These amplifications are typically discontinuous and complex in structure, suggesting that multiple oncogenes in this chromosomal segment may be co-selected during breast carcinogenesis. By integrative analysis of public genomic datasets of breast cancers from the cancer genome atlas (TCGA) including 910 tumor cases and 981 normal controls, we have found that *FOXK2* in 17q25 displayed frequent genomic amplifications and correlated gene expression changes in all subtypes of breast cancers classified by PAM50 compared to normal controls. Its overexpression was associated with poor overall survival of breast cancer patients. *FOXK2* knockdown using lentivirus mediated shRNAs inhibited breast cancer cell proliferation and anchorage-independent growth in four breast cancer cell lines with high *FOXK2* expression status (MDA-MB-231, MCF-7, HCC1954 and MDA-MB-361). More importantly, overexpression of *FOXK2* and oncogene RAS induced MCF10A cell colony formation, indicating that *FOXK2* is an oncogene in breast cancer. The potential interacting molecules/pathways were explored using RNASeq technique on the *FOXK2* knockdown breast cancer cells. Several pathways, including regulation of cell proliferation, regulation of cell division, cell adhesion and regulation of cell metabolism, were regulated by *FOXK2* in breast cancer cells. Our data provide compelling evidence that *FOXK2* is an oncogene in breast tumorigenesis, and it might be a novel therapeutic target and a biomarker predicting poor outcome The chromosome 17 is a frequent site of cancer-associated genetic anomalies and is strongly associated with poor prognosis. Previous studies of breast cancer have revealed the amplification of several genomic regions on 17q. These amplifications are typically discontinuous and complex in structure, suggesting that multiple oncogenes in this chromosomal segment may be co-selected during breast carcinogenesis. By integrative analysis of public genomic datasets of breast cancers from the cancer genome atlas (TCGA) including 910 tumor cases and 981 normal controls, we have found that *FOXK2* in 17q25 displayed frequent genomic amplifications and correlated gene expression changes in all subtypes of breast cancers classified by PAM50 compared to normal controls. Its overexpression was associated with poor overall survival of breast cancer patients. *FOXK2* knockdown using lentivirus mediated shRNAs inhibited breast cancer cell proliferation and anchorage-independent growth in four breast cancer cell lines with high FOXK2 expression status (MDA-MB-231, MCF-7, HCC1954 and MDA-MB-361). More importantly, overexpression of *FOXK2* and oncogene RAS induced MCF10A cell colony formation, indicating that *FOXK2* is an oncogene in breast cancer. The potential interacting molecules/pathways were explored using RNASeq technique on the *FOXK2* knockdown breast cancer cells. Several pathways, including regulation of cell proliferation, regulation of cell division, cell adhesion and regulation of cell metabolism, were regulated by *FOXK2* in breast cancer cells. Our data provide compelling evidence that *FOXK2* is an oncogene in breast tumorigenesis, and it might be a novel therapeutic target and a biomarker predicting poor outcome.

Biography

Amy Hong Zhang is an Associate Professor in the Department of Pathology and Translational Molecular Pathology in University of Texas-MD, Anderson Cancer Center in Houston, TX she is an American Board certified practicing Pathologist since 2003. She has expertise in diagnosing breast cancers and the interpretation of the biomarkers relevant to breast cancers for patient care. She is also actively supervising research scientists and trainees on translational and laboratory research, focusing on the characterization of tumor markers significant for breast tumorigenesis and the development of small molecule inhibitors and potential novel molecular targets for breast cancer treatment.

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Circadian/melatonin disruption by dim light at night drives human epithelial breast cancer to a metastatic phenotype

Steven M Hill, Xiang S, Dauchy RT, Wren-Dail MA, Abdelegan M, Rowan B and **Blask DE**
Tulane University School of Medicine, USA

Cancer patients with disrupted 24-hour (circadian) rhythms are reported to have poorer survival as compared to those with normal rhythms. We have reported that circadian/melatonin (MLT) disruption by exposure to dim light at night (dLAN) resulted in constitutive activation of ERK1/2, STAT3, and signaling nodes involved in epithelial to mesenchymal transition (EMT) in breast tumor xenografts promoting drug-resistance and that MLT can suppress the invasive activity of metastatic breast cancer. This study examined the scientific premise that dLAN-induced circadian/MLT disruption promotes EMT of epithelial MCF-7 breast tumor xenografts leading to the development of metastatic foci in the lungs, livers, and brains of circadian complete (MLT-producing) athymic nude female rats and mice. Employing athymic nude female rats and mice with ERa+ MCF-7 luciferase expressing tumor xenografts housed in LD, 12:12 (nighttime MLT) and LD, 12:12dLAN (dLAN) photoperiods or in dLAN supplemented with night time MLT, tumor from rats in dLAN showed increased growth and expression of signaling nodes involved in promoting EMT and metastasis vs. those from rats in LD: 12:12 dLAN+MLT or LD, 12:12. Nude mice exposed to dLAN showed metastatic outgrowth of MCF-7Luc xenografts forming identifiable metastatic foci in the lungs, livers, and brains of all mice, which was inhibited by MLT, as measured by IVIS small animal imaging system. CRISPR knock out of the MT1 MLT receptor in MCF-7 breast cancer cells induced a 9-fold increase in invasion as compared to parental control cells. This study is the first to show that circadian/MLT disruption by dLAN cab drive EMT and metastasis.

Biography

Steven M Hill received his PhD from the University of Arizona School of Medicine and Postdoctoral studies under Dr William L McGuire at The University of Texas Health Science Center in San Antonio. He is a Professor in the Department of Structural and Cellular Biology, the Edmond and Lily Safra Chair for Breast Cancer Research, and then Director of the Tulane Center for Circadian Biology at Tulane University School of Medicine. He has published more than 100 peer-reviewed papers in reputed journals and has been serving on the Editorial Board of the Journal of Pineal Research and Frontiers in Endocrinology.

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The impact of nolvadex to generic tamoxifen switch on side effects and patient compliance in hormone receptor positive breast cancer patients

Bashar Zeidan, Karen Anderson, Lashan Peiris, Dick Rainsbury and **Siobhan Laws**
Royal Hampshire County Hospital, England

Introduction: Adjuvant hormonal therapy in oestrogen receptor (ER) positive breast cancer patients improves survival. In 2006 the original tamoxifen preparation (Nolvadex) was discontinued and patients were since gradually switched to alternative generic tamoxifen brands. The goal of this study is to evaluate factors affecting adjuvant tamoxifen related side effects and compliance including altering tamoxifen products.

Methods: Consecutive patients treated for ER positive breast cancer (stage I-III) in the Royal Hampshire County Hospital between January 1, 2007 and December 31, 2009 were included. 327 questionnaires were sent to eligible patients. Pearson's χ^2 test was used for data analysis.

Results: 59% of patients experienced side effects associated with tamoxifen treatment out of which 53% were severe. Switching to generic tamoxifen was associated with more severe side effects (p=0.02). Non-prescribed supplements were taken by 42% of symptomatic patients with no significant improvement (p=0.05). Interestingly, the concomitant use of SSRI had no effect on side effects experienced by patients. A significant number of patients considered discontinuing tamoxifen because of the side effects (p=0.001), yet this did not translate into tamoxifen discontinuation or non adherence (p=0.8 and 0.08 respectively).

Conclusions: Severe tamoxifen side effects are commonly experienced by breast cancer patients and are altered by change in tamoxifen brand. Most patients will continue to take tamoxifen despite these side effects following clinicians' advice to avoid cancer relapse. Supplementation and antidepressants did not improve tamoxifen related side effects. Further studies are needed to validate our preliminary findings.

Biography

Bashar Zeidan is a Clinical Lecturer in Surgery at the University of Southampton. He has a special interest in breast cancer research and oncoplastic breast surgery. He was awarded the first UK Academic Clinical Fellowship in Surgery in 2007. Following his fellowship he completed a higher degree focusing on breast cancer research and was granted a Doctorate of Philosophy Degree from the University of Southampton in 2013. He is an author of more than 15 papers and 2 book chapters in the field of surgery.

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Adverse effects of non-hormonal pharmacological interventions in breast cancer survivors, suffering from hot flashes: A systematic review and meta-analysis

Jill Brook Hervik
Vestfold Hospital Trust, Norway

Purpose: To access frequency and severity of adverse effects (AE) of non-hormonal drugs (NHD) for hot flashes in breast cancer survivors compared to controls and analyze adverse effect risk by reviewing published randomized trials.

Methods: Five data bases were searched, trials were included where participants were breast cancer survivors suffering from hot flashes, treatment was self-administered venlafaxine, gabapentin or clonidine, and AE's were reported. AE frequency and severity was graded and a meta-analysis with sub-group analyses was conducted.

Results: 12/49 studies were included, 1467 participants experienced 772 adverse effects, 81% from treatment groups and 19% from control groups. 67% of AE's was graded as mild and 33% as moderate. The frequency of AE for NHD was overall significant versus placebo. AE frequency and severity increased at higher doses for venlafaxine and gabapentin compared to placebo.

Conclusion: The odds for experiencing AE was significantly higher in patients randomized to high dose NHD than those randomized to controls, including placebo, low dose medication and acupuncture. These therapies should be considered as a potential treatment alternative.

Biography

Jill Brook Hervik is currently working as a Physiotherapist, Acupuncturist and Researcher in hospital pain clinic (Vestfold Hospital Trust, Norway). Her areas of interest include integrative medicine, the importance of detailed clinical examination, multidisciplinary approach to pain syndromes and long term side effects of breast cancer treatments. She has published eight different articles in reputable medical journals.

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Volkmann's breast operation (modified radical mastectomy) and its value in modern treatment of breast cancer

Valerijus Ostapenko
National Cancer Institute, Lithuania

Introduction: We have an insufficient scientific data about pre-Halstedian (1867/1875 - 1894) period of breast cancer history, about the results of breast cancer treatment. The primary aim of this article is to present authentic scientific data about pre-Halstedian period of breast cancer history, evaluate the value of this period and the results of breast cancer treatment. The secondary aim of this article was to compare the 3-year retrospective results of Volkmann's breast operation (according to our day lexicon-modified radical Madden mastectomy) with 3-year retrospective results of radical Halsted-Meyer mastectomy.

Methods: This article is based on the original papers, and the authentic manuscripts of the European and the American scientists of the end of XIX -beginning of the XX century with their images, and images of breast operations.

Results: According to presented data, in pre-Halstedian period, Volkmann's operation, become the gold standard of breast cancer treatment. During 20-25 years, initial 3 year results of Volkmann's operation were significantly improved from 17.8%-23 % in 1880/1881 to 35%-45% in 1894/1904. During 30 years, the initial 3year results of radical (Halsted-Meyer) mastectomy were refined from 45% in 1889-1894 to 26.6%-32.2% in 1931. Retrospectively, the latest results of Volkmann's operations with regular dissection of axilla were similar with the results of radical Halsted mastectomy. In 1965, Madden presented modified radical mastectomy with removing breast, pectoral fascia, dissection of axillae and preserving pectoral muscle and reintroduced Volkmann's operation. Even today, modified radical (Madden) mastectomy – Volkmann's operation is a standard of breast cancer treatment.

Conclusion: The period of pre-Halstedian breast cancer history, the results of classic Volkmann's breast operation, the names of prominent European and American surgeons were forgotten, and our duty is to reintroduce it.

Biography

He defended his doctoral dissertation "Plastic and reconstructive surgery corrective sergančiosioms ikinavikinėmis breast disease and breast cancer", in 2000 - a doctoral thesis habilitation "in patients with breast cancer and ikinavikinėmis disease treatment. Dissertations detailed analysis of the combined results of treatment of breast cancer, and made recommendations to patients treated with improving the quality of life. V. Ostapenko the chief researcher, together with co-authors published more than 118 scientific papers, 4 rationalization proposals author. Actively participate and present reports in international oncologists and plastic reconstructive surgeons congresses held in the Baltic countries, Poland, Russia, Greece, Austria, Australia, Portugal, Belgium, Canada, the United States.

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The use of high dose estrogens for the treatment of breast cancer

Carole Verhoeven
Pantarhei Oncology BV, The Netherlands

Efficacy of estrogens for treatment of advanced breast cancer was first described by Haddow in 1944. Results of Haddow were a paradox, as breast cancer was considered to be dependent on estrogens for growth. In the following years research on high dose estrogens (HDEs) was continued, making estrogens the standard of care in postmenopausal women with advanced breast cancer. In the 1970s, estrogen therapy was replaced by tamoxifen. Although not more effective than HDEs, tamoxifen was less toxic and therefore considered to be the preferred agent. In the 1990s, estrogen therapy has gained new interest as clinical studies showed anti-tumor efficacy with different estrogens (DES, EE, E2) in heavily pre-treated postmenopausal women in an estrogen deprived setting. The fact that estrogens can be used to treat breast cancer has almost been forgotten. Therefore, a review paper has been published, summarizing all literature data on this topic. The success of estrogen therapy is dependent on the menopausal status and how long the patient has been deprived of estrogens (gap hypothesis). Research on mechanism of action has shown that apoptosis induced by estrogens is regulated via the estrogen receptor. HDEs have a negative safety reputation, especially of having side effects related to the cardiovascular system. The fetal estrogen estetrol might be a new treatment option as estetrol has less interference with liver function as compared to other estrogens. A proof of concept study is ongoing in Germany to assess safety and anti tumor efficacy of estetrol in postmenopausal women with advanced ER+ breast cancer.

Biography

Carole Verhoeven is a PhD holder. She is the Chief Scientific Officer (CSO) at Pantarhei Oncology BV, the company developing estetrol for the treatment of breast and prostate cancer. She has studied Chemistry at the Catholic University of Nijmegen (1989) and received her PhD on the metabolism of structurally related synthetic steroidal hormones in 2001 from the University of Groningen. From 1994-2011 she has been working for Organon/Schering-Plough/MSD in several positions in preclinical and clinical development. She has published 24 scientific papers in peer-reviewed journals.

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Exclusive self-destruction of triple negative breast cancer cells

Cohen-Armon
Tel-Aviv University, Israel

A newly - discovered mechanism involves the modification of specific proteins that affect the construction and stability of the spindle structure during mitosis. Their exclusive modification in human cancer cells prevented chromosomes segregation into daughter cells. Modifications of kinesins and NuMA, preventing their normal activity in the spindle of human cancer cells disrupted chromosomes alignment in the spindle mid-zone. This induces a rapid cell self-destruction while mitosis is prevented. Thus, the faster the cancer cells proliferate, the more quickly they die. Research was conducted using both cancer cell cultures and mice transplanted with human cancer cells. Mice transplanted with triple negative breast cancer cells revealed the arrest of tumor growth by agents causing their exclusive cell-death during mitosis, without affecting normal proliferating cells.

Biography

Cohen-Armon working in an Academic position at the Tel-Aviv University Life Science, Neurobiochemistry and Faculty of Medicine, Dept. of Physiology and Pharmacology and the Sagol School of Neuroscience . In 2001, she was appointed as visiting researcher in Columbia University, New York. She conferred with Human Frontiers award. She has published more than 30 papers in well reputed and high impact factor journals since 2000. Her research was supported by Novartis and the active molecule is prepared for use against triple negative breast cancers. She is an academic editor for several journals. Her interest lies in Signal transduction and Epigenetic mechanisms, protein modifications, drug discovery.

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A functional cross-talk between GPER and IGF1/IGF1R signaling drives breast tumor angiogenesis via activation of the HIF-1α/VEGF transduction pathway

De Francesco EM, Maggiolini M, Sotgia F, Lisanti MP and **Clarke RB**
University of Manchester, UK

Compelling experimental evidence indicate that a member belonging to the G-protein coupled receptor superfamily, named GPER/GPR30, acts as a receptor for estrogens in diverse physio-pathological conditions, including breast cancer. Furthermore, GPER signaling has been shown to mediate stimulatory responses in breast cancer associated fibroblasts (CAFs), which are key components of the tumor microenvironment driving disease progression. In this context, we have recently demonstrated that GPER is involved in breast cancer cells adaptation to hypoxic microenvironment, through the activation of HIF-1α/VEGF transduction pathway and the angiogenic response. Worthy, a functional cross-talk between GPER- and growth factor (EGF, insulin and IGF1)-signaling has been demonstrated to integrate complex biological events in breast cancer, like cell proliferation and migration. Here, we evaluate the angiogenic-promoting role of GPER through the regulation of VEGF expression and function triggered by IGF1. Using estrogen receptor (ER)-negative and GPER positive SkBr3 breast cancer cells and CAFs derived from mammary ductal carcinomas, we demonstrate that IGF1 activates through IGF1R the ERK1/2 and AKT cascades, leading to the increase of HIF-1α and its targets GPER and VEGF. RT-PCR, western blotting, immunofluorescence and reporter assays, gene silencing strategies and in vitro angiogenesis studies show that a functional cross-talk between HIF-1α and GPER regulates VEGF expression and function, toward new blood vessel formation in breast cancer. Taken together, our findings demonstrate that targeting the interactions between GPER and IGF1/IGF1R may represent an innovative strategy for halting the angiogenic response in breast cancer.

Biography

De Francesco EM has completed her PhD in 2013 at the University of Calabria, where she has been involved in the characterization of estrogen signaling through GPER since 2009. She has published more than 25 papers in reputed journals and she has joined the University of Manchester in 2015, where her research is currently supported by an EU and AIRC (Associazione Italiana per la Ricerca sul Cancro) co-funded fellowship.

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FoxM1 inhibition: A novel therapeutic avenue to treat breast cancers

Manjeet Rao
University of Texas Health Science Center, USA

Defect in DNA damage response serves as a major factor predisposing normal cells to acquire oncogenic mutations. However, after tumor develops, cancer cells manage their survival by repairing DNA damage resulting from unchecked DNA replication. Moreover, the ability of cancer cells to repair chemotherapy-induced DNA damage also serves as one of the mechanisms for therapy resistance. Therefore, successful targeting of factors/pathways that are capable of inducing DNA damage and suppressing DNA repair responses of cancer cells will have promising therapeutic outcomes. We recently discovered that imipramine blue (IB), a novel analogue of anti-depressant imipramine that we recently synthesized, induces DNA damage and inhibits the ability of breast cancer cells to repair DNA. Using an innovative ex-vivo model of tumor explants from breast cancer patients, we demonstrate that IB inhibits breast cancer growth without affecting normal mammary epithelial cell proliferation. Notably, our studies revealed that systemic delivery of IB using nanoparticle-based drug delivery approach suppressed breast cancer growth and metastasis without inducing any toxicity in pre-clinical mouse models. Furthermore, our in vitro studies show that IB may improve the efficacy of doxorubicin and paclitaxel, a chemotherapeutic drug combination that is routinely used to treat TNBC patients. Importantly, our drug-interaction results suggest that IB may directly bind to and inhibit the activity of proto-oncogene FoxM1 and subsequently alter FoxM1-associated signaling that play critical roles in DNA repair and are known to mediate taxol resistance. We believe that our study will set the stage for a new paradigm of treating breast cancers using IB therapeutic. Our preliminary studies showing inhibition of breast cancer growth in orthotopic mouse model and explants from breast cancer patients by IB without targeting normal mammary epithelial cells suggest that IB may serve as a novel therapeutic with negligible toxicity. Since FoxM1 has been proposed to be a bonafide therapeutic target for several cancers including non-breast cancers, identification of a compound like IB that inhibits FoxM1 and FoxM1-dependnet mechanisms has immense translational potential for treating many aggressive cancers.

Biography

Manjeet Rao has completed his PhD from University of Delhi and Postdoctoral studies from MD Anderson Cancer Center, Houston, TX, USA. He is an Associate Professor at Greehey Children's Cancer Research Institue, University of Texas Health Science Center, San Antonio. He has published more than 38 papers in reputed journals including cell, PNAS, blood, leukemia, oncogene and clinical cancer research.

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The effect of internet-based breast cancer patient's pathway on breast cancer patients' empowering process

Anne Ryhänen
The University of Turku, Finland

This study was conducted to examine the effect of the breast cancer patient's pathway program (BCPP) on breast cancer patients' empowering process. The ultimate goal of this study was to develop breast cancer patient education in a more empowering direction by using the patient pathway as a patient education tool. The BCPP is an internet-based patient education program. The structure of the BCPP is based on a flow chart diagram picture of the patient pathway during the breast cancer care and treatment process and used with oral and written patient education. Newly diagnosed breast cancer patients were randomized to an intervention group (n=50) and control group (n=48). The patients' knowledge expectations, perceptions of received knowledge, knowledge level, quality of life, anxiety, and treatment-related side effects were measured during the breast cancer treatment process. Breast cancer patients' perceptions of received knowledge were not fulfilled; their knowledge expectations exceed the perceived amount of received knowledge. Statistical differences were not found between the groups in terms of quality of life, anxiety and treatment-related side effects. However, anxiety decreased faster in the intervention group when looking at internal differences between the groups at different measurement times. In the intervention group the relationship between the difference between knowledge expectations and perceptions of received knowledge correlated significantly with quality of life and anxiety. Their knowledge level was also significant higher than in the control group. These results support the theory that the empowering process requires patient's awareness of knowledge expectations and perceptions of received knowledge.

Biography

Anne Ryhänen has completed her PhD from University of Turku. She is the Director of Nursing in Turku City Hospital and the Clinical Teacher in Department of Nursing Science in the University of Turku. She has published more than ten papers in reputed journals. She is a Member of Empowering Patient Education research group, where she is making her postdoc study.

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Relationships among body mass index, systemic immune-inflammation index and luminal subtype in the resistance to endocrine therapy of breast cancer

Qing-xia Li, Dong-jian Shi, Li Li, Jing Zhao, Li-xia Zhang, Na Li, Xin-na Deng and **Jian-hui Cai**
Hebei General Hospital, China

Breast cancer is the most common cancer for women worldwide. Endocrine therapy has become one of the most important treatment options for hormone-sensitive patients, which accounts for approximately 70-80% of breast tumors. Many studies have explored the effect of high BMI on breast cancer patients with endocrine therapy, but the treatment efficacy is not clear in China. The relationships among BMI, SII and luminal subtype in endocrine therapy of breast cancer have been rarely explored .We analyzed the data from 161 breast cancer patients ,and demonstrated that the 5-year resistance rates of the patients in high BMI group and high SII group are significantly higher than that in the normal BMI group and low SII group, indicating that BMI and SII are closely related to endocrine therapy resistance of luminal type breast cancer. Further analysis shows that BMI and SII reveal the significantly positive correlation, suggesting that the increase of BMI may promote the increase of SII in a certain way, and both are involved in the resistance to endocrine therapy.BMI and SII can be the indicators for the prognosis of luminal type breast cancer, which can not only improve prognostic accuracy, but also reduce the physical pain and cost toxicity for patients.

Biography

Qing-Xia Li has completed her PhD from The Fourth Military Medical University. She is the Associate Director of the 4th Department of Oncology, Hebei General Hospital. She has published more than 40 papers in reputed journals and has been serving as an Editorial Board Member of repute.

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Sessions

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Screening, Detecting, and Diagnosing Breast Cancer | Surgery Choices for Breast Cancer | Personalized Medicine for Breast Cancer Treatment

Session Chair
Uhi Toh
Kurume University School of Medicine, Japan

Session Co-chair
Anne Ryhanen
The University of Turku, Finland

Session Introduction

Title: **Comparison of bilateral whole-breast ultrasonography versus magnetic resonance imaging in the setting of breast cancer staging**

Hongying He, University of Texas Health Science Center at Houston, USA

Title: **Oncoplastic and reconstructive surgery single institution experience**

Zhygulin Andrii, LISOD Israeli Cancer Care Hospital, Ukraine

Title: **Real-time indocyanine green (ICG) fluorescence imaging technique for the detection of SLNs in early-stage breast cancer**

Uhi Toh, Kurume University School of Medicine, Japan

Title: **Proteomic profiling of plasma and tissue proteins associated to mammographic breast density using the KARMA cohort**

Marike Gabrielson, Karolinska Institutet, Sweden

Title: **Breast cancer in young women-Retrospective study**

Jana Slobodnikova, Alexander Dubcek University of Trencin, Slovakia

Title: **E-MPBC-imaging findings of a rare aggressive breast cancer subtype: Metaplastic carcinoma of the breast**

Hale Aydin, Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Turkey

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Comparison of bilateral whole-breast ultrasonography versus magnetic resonance imaging in the setting of breast cancer staging

Hongying He
University of Texas Health Science Center at Houston, USA

Objective: To compare the incremental cancer detection rate (ICDR) using bilateral whole-breast ultrasonography (BWBUS) versus dynamic contrast-enhanced magnetic resonance imaging (MRI) in patients with primary breast cancer.

Methods: A retrospective database search in a single institution identified 259 patients with breast cancer diagnosed from January 2011 through August 2014 who underwent mammography, BWBUS, and MRI before surgery. Patient characteristics, tumor characteristics, and lesions seen on each imaging modality were recorded. The sensitivity, specificity, and accuracy for each modality were calculated. ICDRs according to index tumor histology and receptor status were also evaluated. The effect of additional cancer detection on surgical planning was obtained from the medical records.

Results: A total of 266 additional lesions beyond 273 index malignancies were seen on at least one modality, of which 121 (45%) were malignant and 145 (55%) benign. MRI was significantly more sensitive than BWBUS (p=0.01), while BWBUS was significantly more accurate and specific than MRI (p<0.0001). Compared with mammography, the ICDRs using BWBUS and MRI were significantly higher for estrogen receptor-positive and triple-negative cancers, but not for human epidermal growth factor receptor-2-positive cancers. Twenty-two additional malignant lesions in 18 patients were seen on MRI only. Surgical planning remained unchanged in eight (44%) of those 18 patients.

Conclusion: MRI was more sensitive than BWBUS, while BWBUS was more accurate and specific than MRI. MRI-detected additional malignant lesions did not change surgical planning in almost half of these patients. BWBUS may be a cost-effective and practical tool in breast cancer staging.

Biography

Dr. Hongying He completed her PhD in microbiology at State University of New York at Buffalo in 2000 and her MD at Albert Einstein College of Medicine in New York City in 2005. She completed her radiology residency in the McGovern Medical School at UT Health in 2010 and her breast imaging fellowship at M.D. Anderson Cancer Center in 2011. She is currently the Chief of Breast Imaging in the Department of Diagnostic and Interventional Imaging at the McGovern Medical School. Her main research interest includes correlating imaging features of breast cancer with underlying biology and clinical outcomes.

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Oncoplastic and reconstructive surgery single institution experience

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Introduction: Breast conserving surgery (BCS) followed by radiation therapy and skin-sparing mastectomy with immediate reconstruction (IR) have proven their efficiency and safety. The technical and oncological aspects of breast oncoplastic surgery in our breast unit, organized according EUSOMA criteria are presented.

Materials & Methods: Treatment was carried out on multidisciplinary tumorboard. During BCS we used therapeutic mammoplasties or flaps from the chest, abdominal wall, LICAP-flaps or LD-flaps. In case of mastectomy we offered immediate reconstruction. Type of reconstruction was chosen according clinical situation. Photos of the patients were performed.

Results: From 2007 to 09.2016 1032 surgeries in 715 patients were performed. 400 oncoplastic BCS were performed in 392 patients. Average age was 53.2(22-88), tumor size – 2,15cm (0, 8-15), weight of specimen - 109g (6-1034). We used therapeutic mammaplasties in 140 (35.0%) cases, local chest wall flaps - in 93 (23.3%). Complications had 102(25.5%) patients. We followed up 342 (87.2%) patients during 35.5 (6-108) months. Local recurrence occurred in 8(2.3%) patients. 35(10.2%) patients had metastasis, 18(5.3%) of them died. In IR group 148 immediate reconstructions were performed in 123 patients. The average age was 45 (29-71).We did 68 (45.9%) one-stage reconstructions, 26(17.5%) - with ADM, 17(11.5%) - with synthetic mesh. Two-stage surgeries were done in 56(37.8%) cases. LD-flap was done in 9(6.8%) patients, LD-flap + implant - in 11(7.4%), pedicled TRAM-flap - in 4(2.7%). Skin-sparing mastectomy was performed in 30(20.3%) patients, skin-reducing - in 38(25, 7%), nipple-sparing in 55(37,2%). We followed up 103(83.7%) patients during 32 months (6-84). Local recurrence was found in 1(0.9%) patient, distant metastases - in 17(16.5%) and 6(5.8%) of them died. Early complications were found in 51(34.4%) cases.

Conclusions: We evaluated our experience in oncoplastic BCS and reconstructive surgery in a dedicated BU that would allow for radical treatment with excellent aesthetical outcomes.

Biography

Zhygulin A V is a Physician, general and oncological surgeon, breast and reconstructive surgeon. He is the Founder and Chief of the first in Ukraine regular twice a year two-week intensive educational course of Oncoplastic and reconstructive surgery and modern breast cancer treatment for the breast surgeons, Kyiv, Ukraine and Founder of Ukainian International breast conference, Kyiv, Ukraine (2014, 2015 and 2016). He has been serving as a Head of Breast Unit in LISOD Israeli Cancer Care Hospital, Kyiv, Ukraine, the first in Ukraine appropriate EUSOMA criteria (Full Membership of Breast Centers Network since 2013) since 2011. He is the Member of ESSO.

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Real-time indocyanine green (ICG) fluorescence imaging technique for the detection of SLNs in early-stage breast cancer

Uhi Toh and **Yoshito Akagi**
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Background: The sentinel lymph nodes status of breast cancer is used to predict the status of the remaining axillary lymph nodes accurately and sentinel lymph node biopsy (SLNB) provide staging information and to determine the need for axillary lymph node dissection in breast cancer patients. The purpose of this study was to evaluate the utility of a color charge-coupled device (CCD) camera system for the intraoperative detection of SLNs and to determine its clinical efficacy and sensitivity in patients with operable breast cancer.

Methods: The intraoperative detection of SLNs was performed using the conventional Indigo Carmine dye (indigotindisulfonate sodium) technique combined with a new Indocyanine green (ICG) imaging system (HyperEye Medical System: HEMS, MIZUHO IKAKOGYO, Japan) to map SLNs, in which the lymphatic vessels and SLNs were visualized transcutaneously with illuminating ICG fluorescence. One intradermal injection of 3.5ml indigo carmine (blue dye) mixed with 0.5ml indocyanine green (ICG) was performed via the subareolar plexus followed by 5 minutes breast massage for dilating breast lymphatics. After an inferior axillary incision, the search of SLN was guided by HEMs for lighting stained lymphatic channels leading to blue-stained LNs.

Results: Between January 2012 and May 2013, SLNs were successfully identified in all 168 patients (detection rate: 100%). By histopathology, the sensitivity was 93.8% for the detection of the metastatic involvement of SLNs (15 of 16 nodal-positive patients). Immunohistology revealed one false-negative case among 16 patients (6.3%). After a median follow-up of 30.5 months, none of the patients presented with axillary recurrence.

Conclusion: These results suggest that the HEMS imaging system is a feasible and effective method for the detection of SLNs in breast cancer. Furthermore, the HEMS device permitted the transcutaneous visualization of lymphatic vessels under light conditions, thus facilitating the identification and detection of SLNs without affecting the surgical procedure, together with a high sensitivity and specificity.

Biography

Uhi Toh has completed his MD and PhD from Kurume University School of Medicine. He is currently working as the Associate Professor of Department of Surgery and the Director of Breast Surgery of Kurume University Hospital. He has published more than 50 papers in reputed journals.

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Proteomic profiling of plasma and tissue proteins associated to mammographic breast density using the Karma cohort

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Following age, mammographic density (MD) is considered one of the strongest risk factors for breast cancer. Despite the association between MD and breast cancer risk, little is known about the underlying histology and biological basis of breast density. To better understand the mechanisms behind MD we conducted large-scale proteomic analyses of blood plasma using two sample sets comprising 729 and 600 women, and assessed morphology, proliferation and hormone receptor status through immunohistochemical staining in breast tissues from 160 women. Plasma and tissue protein expressions and morphology was assessed in relation to absolute area-based breast density. All samples were collected from non-diseased women as part of the KARMA (Karolinska mammography project for risk prediction for breast cancer) project. The KARMA study is a population-based prospective cohort with the overarching goal to reduce the incidence and mortality of breast cancer by focusing on individualized prevention and screening. Plasma profiling revealed 20 proteins with linear associations to MD. These proteins have previously been described in processes of tissue homeostasis, DNA repair, cancer development and/or progression in MD. In breast tissue, high MD was associated with higher amount of stroma and epithelium and less amount of fat, but was not associated with a change in epithelial proliferation or receptor status. Increased expression of both epithelial progesterone receptors and stromal oestrogen receptors was associated with a greater proportion of stroma, suggesting hormonal involvement in regulating breast tissue composition. Our current data is indicative of the mechanistic processes underlying MD and provide insights into the aetiology of MD as a prominent risk factor for breast cancer.

Biography

Marike Gabrielson has completed her PhD in experimental breast cancer studies in 2013 from the University of Örebro, Sweden, and is currently conducting Postdoctoral studies at Karolinska Institutet in Stockholm, Sweden. She is part of the KARMA study scientific board. She is also Project Manager of tissue collection and experimental work with the overarching goal to identify protein and hormone markers of mammographic density and breast cancer risk.

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Breast cancer in young women-Retrospective study

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Breast cancer is the most common malignancy of the female population the incidence is increasing mainly statistically between 50s and 60s, 60s and 70s. Recently, however, we meet more often with the occurrence of breast cancer in women in 30s and significantly between 20 and 40 year. For women this age range is not exist preventive or screening mammography, in Slovakia only sonography and only clinical self- examination by touch. The period from 1.5.2005 and 30.6.2016 we performed more than 70000 mammography examinations and more than 185000 ultrasound examinations. The youngest patient was 6 months, the oldest 94 years. Patients were sent for examination by attending gynecologist, general practitioner. Preventive examinations completed asymptomatic women without clinical symptoms. Young women and girls were examined by ultrasound with 18 MHz linear proge, with CFM and elastography. Next if necessary, we performed mammography, MR-mammography a CCB too. During the monitored period we diagnosed 398 new cases of the breast cancer, all cases are verified by histopathology. The age distribution of patients with newly diagnosed cancer we transparently stored in tables and graphs. We focused on women in the age group to 39 and 49 year old. In category women between 18s and 39s we diagnosed 32 new cases of breast cancer, between 40s and 49s 64 cases. Summary are 86 of new cases of the breast cancer in women between 18 and 49 years. We analyzed the different findings, especially with respect to possibility of diagnostic self-examination, combined with ultrasound, MR mammography, mammography and core cut biopsy under ultrasound control. The number of the young women with new diagnosed breast cancer slowly increased. Our aim is the early diagnostics, without vascular cancer vascular invasivity, without the lymphadenopathy. We retrospectively focused on genetic anamnesis factor, short time of the diagnosis and therapy.

Biography

Jana Slobodnikova has done her MD from Prague Charles University. She has completed CSc/PhD from Institus of experimental Oncology Slovac Scientic Academy. She also worked as an Ass. Prof. Trnaviensis University. She has published more than 90 scientific papers, from then 25 papers in reputed journals and has been serving as an Editorial Board Member of repute. She has published 3 monographs. She is President of the section of breast imaging of Slovak Radiologic Society and Vice President of the Slovak Society of Ultrasound in Medicine.

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E-MPBC-imaging findings of a rare aggressive breast cancer subtype: Metaplastic carcinoma of the breast

Hale Aydin

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Imaging Findings of a Rare Aggressive Breast Cancer Subtype: Metaplastic Carcinoma of the Breast (E-MPBC): Metaplastic breast carcinoma (MPBC) is one of the rarest and generally poorly differentiated invasive breast carcinomas. According to our knowledge MPBC tend to show more benign imaging features, such as round, lobular, oval shape with a predominantly circumscribed contour. We analyzed 65 patients with pathologically proven MPBC between 2004 and 2016. We reviewed patients' medical files and breast imaging records of the all patients. Patients ranged in age from 25 to 88 years (median, 53 years) and 16 patients were younger than 40 years-old. The most common mammographic findings were round shape, micro lobulated margin and high density masses. The most frequent sonographic presentations of MPBC were round shape, angular margin which partially indistinct, hypoechoic and heterogeneous echo pattern and no posterior feature masses. MRI was performed in 7 patients, and all lesions were presented as masses rather than non-mass enhancements. Six of the lesions showed irregular or speculated margins. Signal intensity-time curves were type-II or type-III. DWI was obtained in 3 patients and the lesions showed diffusion restriction in 2 patients. In conclusion, well-recognizing the findings of MPBC is very important. Because, according to previously reported series this aggressive, high grade tumor can display more benign imaging feature. This appearance can cause misdiagnosis as benign breast lesion especially in young women. Although the lesions demonstrate benign or moderately malign feature, MPBC should be kept in mind in differential diagnosis for large palpable breast masses.

Biography

Hale Aydin has graduated from Ankara University School of Medicine, Ankara and completed residency from Baskent University School of Medicine Ankara (Turkey). She is a Radiologist with sub-specialty expertise in breast imaging, and she has been serving as breast Radiologist at Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara. Her research interests are focused on the use of imaging methods on breast cancers.

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Enhancement of radiosensitivity of human endothelial and breast cancer cells with melatonin by regulating angiogenesis and genes involved in estrogen biosynthesis

Alicia González-González, Alicia González, Carolina Alonso-González, Carlos Martínez-Campa, Javier Menéndez-Menéndez and **Samuel Cos**
University of Cantabria, Spain

Enhancing the radiosensitivity of cancer cells is one of the most important goals in clinical radiobiology. Melatonin exerts oncostatic effects on breast cancer by reducing estrogen biosynthesis in human breast cancer cells, surrounding fibroblasts and endothelial cells and by regulating cytokines that influence tumor microenvironment. This hormone also has antiangiogenic activity in tumoral tissue. Vascular endothelial growth factor (VEGF) produced from tumor cells is essential for the expansion of breast cancer. Thus, the aim of the present study was to investigate whether melatonin sensitizes endothelial cells to radiotherapy by regulating angiogenesis and estrogen biosynthesis. To accomplish this we used cocultures of HUVEC cells with MCF-7 cells. The expression of genes was analyzed by RT-PCR. Cell proliferation was measured by the MTT method, the migration of HUVECs was measured by the wound healing assay and tubulogenesis studies were performed in a tubulogenesis multiplate system in vitro. Only the presence of malignant epithelial cells in the cocultures altered proliferation, the expression of genes involved in the local biosynthesis of estrogens and VEGF, in endothelial cells. In addition, ionizing radiation decreased cell proliferation and VEGF expression, and melatonin pretreatment 1 mM led to a significantly greater decrease. Furthermore, the migration of endothelial cells and the tube formation were reduced with the radiation and melatonin pretreatment resulted in a significantly higher reduction. Our results demonstrate that melatonin could exert a cooperative enhancement of radiosensitivity associated with the modulation of angiogenesis and local estrogen biosynthesis.

Biography

Alicia González González is a PhD student from Cantabria University School of Medicine. Currently, she is involved in breast cancer research and melatonin, specifically in the sensitizing effects of melatonin to chemotherapy and radiotherapy for its antiangiogenic and antiadipogenic actions. She has published 2 papers and has presented her work in 5 congress.

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Breast density in Chinese women: Using percentage and area measures from a quantitative technique

Tong Li[1], Lichen Tang[2], Ziba Gandomkar[1], Rob Heard[1], Claudia Mello-Thoms[1], Zhimin Shao[2], Carolyn Nickson[3] and **Patrick Brennan[1]**
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[3]The University of Melbourne, Australia

Breast density (BD) is an independent risk factor for breast cancer but its characteristics are poorly understood in China. This study aims to identify associated factors with BD in Chinese women by using a quantitative method. 84 cancer and 987 cancer-free women were recruited from Fudan University Shanghai Cancer Centre. BD was measured by an automatic algorithm autodensity and expressed in both percentage density (PD) and dense area (DA) format. Pearson tests were performed to exam relationships between density and continuous variables and t-tests were conducted to compare differences of mean density values for categorical variables. Multivariate models were built using variables being statistically significant from the Pearson and t-tests. For cancer-free women, weight and BMI were negatively associated (r=-0.237, r=-0.272) with PD whereas positively associated (r=-0.495, r =-0.520) with DA; age was associated with PD (r=-0.202) and DA (r=-0.086) but did not add any prediction within multivariate models. Lower PD was found within women with secondary education background or below compared to women with tertiary education. For cancer-women, PD showed similar relationships with that of cancer-free women whilst breast area was the only factor that was associated with DA (r=0.739). This is the first time that BD was measured by a quantitative method for Chinese women and important associations were identified for both PA and DA. The findings are very valuable to policy makers being responsible for introducing effective models of breast cancer prevention and diagnosis.

Biography

Tong Li is a PhD candidate at Faculty of Health Sciences, The University of Sydney. Her PhD project is studying breast density and cancer presentations for women in China. This project will be the first study to determine the optimum image technology for policy makers in China who are considering the implementation and implications of a national population-based breast cancer screening program. She published a literature review regarding breast cancer in China last year in Breast Cancer Research and Treatment with an impact factor of 4.

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Oncogenic protein kinase D regulating networks in invasive breast cancer

Yan Liu[1,2], **Jian Li**[1], **Jun Zhang**[1,2], **Shiyi Yu**[1,2], **Lele Wu**[1,2], **Yuzhi Wang**[1,2], **Xue Gong**[1,2], **Chenxi Wu**[1,2], **Xiuxiu Cai**[1,2], **Lin Mo**[3], **Mingya Wang**[1], **Jun Gu**[3], **Zhenghong Yu**[3] and **Liming Chen**[1,2]
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Invasive breast cancer is the leading cause of women mortality. Protein kinase D2 (PRKD2) and PRKD3 but not PRKD1, were implicated to positively contribute to invasive breast cancer growth and progression. In current study, we found that PRKD2 and PRKD3 function as important oncogenic drivers in invasive breast cancer with evidences showing that PRKD2 and PRKD3 were preferentially expressed in invasive breast cancer cells and tissues to promote breast cancer growth in vitro and in vivo. To uncover the molecular mechanisms of PRKD2 and PRKD3 in invasive breast cancer, phosphoproteome, interactome and transcriptome of PRKD2 and PRKD3 were systematically investigated. Besides identification of PRKD2 and PRKD3 regulated phosphoproteins, interacting proteins and target genes expression, 36 hub nodes including known breast cancer drivers, such as TP53, MYC and BRCA1, were identified in PRKD2 and PRKD3 regulating networks. ELAVL1 and UBC were recognized as the most common hub nodes across PRKDs networks. The enriched pathway analysis reveals that PRKD2 and PRKD3 regulated pathways contribute to multiple cancer related events, including cell cycle, apoptosis, migration, angiogenesis, cancer energy metabolism and cancer immunity. Enrichment of cell cycle and cell mobility related pathways across PRKDs networks, explained the observations that depletion of PRKD2 or PRKD3 or both or inhibition of PRKDs activity led to alternation of cancer cell cycle and decrease of cancer cell migration ability. Besides common features, notable variations were also observed from phosphoproteome, interactome to transcriptome between PRKD2 and PRKD3, indicating that PRKD2 and PRKD3 have shared specific functions and mechanisms. Finally, our studies raised promising invasive breast cancer therapeutic drug targets, such as ELAVL1, Ubiquitin system, HDACs and so on. Taken together, the important roles as well as the molecular mechanisms of PRKD2 and PRKD3 in invasive breast cancer were uncovered to provide clues for further combating invasive breast cancer.

Biography

Liu Yan was born in Shandong province, China in 1989. He obtained B.S in Bioscience from Northeast Agriculture University in 2012. Now he is studying PhD degree in southeast University major in oncobiology.

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Evaluation of diffusion weighted MR Imaging and 18F-FDG PET for monitoring triple negative breast cancer response to cisplatin treatment

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Objective: To evaluate the potential of 18F-FDG PET and diffusion weighted MR Imaging (DWI) in predicting response of triple negative breast cancer (TNBC) to Cisplatin treatment.

Methods: Cisplatin (10 mg/kg) was injected one shot intraperitoneally into TNBC tumor bearing mice. Animals were imaged on PET and MRI scanners dedicated to animal use before treatment (day 0) and days 3 and 7 after treatment. The highest standardized uptake value (SUVmax) and the average of apparent diffusion coefficient value (ADCmean) were measured.

Results: We evaluated tumor growth of the non-treated mice (n=8) and treatment mice. Treated mice were divided into the response group (n=7) and the no response group (n=7) based on whether the tumor growth was similar to or slower than that of the non-treated mouse. SUVmax value on day 3 and day 7 (SUV3, SUV7) showed significant difference between the response group and no response group ($P<0.05$), however, ratio of SUVmax on day 7 to day 0 (SUV7/0) showed no significant difference between three groups ($P>0.05$). ADC mean value on day 0 (ADC0) of the response group was significantly lower than that of the no response group ($P<0.01$). The ratio of ADC mean on day 7 to day 0 (ADC7/0) showed significant difference between three groups ($P<0.01$), and ADC7/0 of the response group were significantly higher than those of control group and no response group.

Conclusions: ADC0, ADC7/0 is potential early predictors of response of TNBC to cisplatin treatment..

Biography

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